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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SRIVASTAVA, KAILASH C	
ART UNIT	PAPER NUMBER
1657	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/870,498	LEITE ET AL.	
	Examiner	Art Unit	
	Dr. Kailash C. Srivastava	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7, 17-28 and 31* is/are pending in the application.

4a) Of the above claim(s) *1-4 and 17-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-7 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The response and amendment filed 19 September 2008 to the Office Action mailed 01 May 2008 is acknowledged and entered.

Amendments and Response based Withdrawals

2. In view of remarks and amendments filed 19 September 2008, the following objection and rejection
in the Office Action mailed 18 March 2008 are hereby withdrawn:

- Anticipation rejection to Claims 5 and 7 under 35 U.S.C. §102(b) as anticipated by Hancock et al (US Patent 6,040,435).

Informal Matters

3. In response filed 19 September 2008, reciting number of non-Final rejections; Applicants request intervention by the "Supervisory Primary Examiner" (See, Remarks filed 19 September 2008, Page 7, Lines 7-8).

Please note, contrary to applicants' assertion, the United States Patent and Trademark Office (i.e., USPTO) has a position of Supervisory Patent Examiner, not "Supervisory Primary Examiner". Accordingly, the applicants are reminded about 37 C.F.R. §1.3 Business to be conducted with decorum and courtesy that states, "Applicants and their attorneys or agents are required to conduct their business with the United States Patent and Trademark Office with decorum and courtesy." Please note further that a total of only 5 Non-Final Office Actions have been issued according to the records in IFW File at the USPTO for the instant application. Of said 5 Office Actions, the Office Action mailed 01 May 2008 was the fourth one issued from Examiner Srivastava. Please also note, the Office Action mailed 01 May 2008 was approved by the Supervisory Patent Examiner, Dr. Jon P. Weber. Thus, the Supervisory Patent Examiner is already apprised of the status of the instant Non-Provisional application.

4. Regarding the interview conducted on 06 February 2007, contrary to applicants' remarks in the response filed 19 September 2008, the Interview summary in the Office Action issued 20 February 2007 is an accurate description of items agreed to in said Interview (i.e., it was agreed to withdraw the written description rejection to Claims 5-7 and 29 under 35 U.S.C.§112, first paragraph and Obviousness rejection to Claims 5-7 and 29 under 35 U.S.C. § 103 (a), Additionally, the Applicants were going to cancel Claim 29 to bring the application in a better condition for allowance.) There is no statement of

agreement to allow the application. The box "N/A" was checked because full agreement was not achieved, only partial. Furthermore, in said interview, aside from Examiner Srivastava a Primary Examiner was also present and additionally, as the applicants have acknowledged in their response filed 08 August 2007, in the subsequent Office Action, the rejections under 35 U.S.C. §112 and §103 discussed in the Interview Summary mailed 20 February 2007 were withdrawn. Thus, Applicants' assertion, "Examiner misstates the facts" (See, Remarks filed 19 September 2008, Page 7, Lines 9-10) is incorrect.

5. Contrary to Applicants' Remarks, "Regarding the rejection under 35 U.S.C. §112, Claim 5, and hence all Claims" (See, Remarks filed 19 September 2008, Page 7, Lines 11-13); said rejection in the Office Action
mailed 01 May 2008 is under 35 U.S.C. §112, 1st paragraph (See, Office Action mailed 01 May 2008, Pages 3-4, item 11). Accordingly, Applicants' arguments to said rejection in the Office Action that follows (Please see, items 9-10 of the instant Office Action) will be responded in view of the rejection to Claims 5-7 and 31 under 35 U.S.C. §112, 1st paragraph for lack of written description, and enablement with respect to the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with those claims.

6. The instant non-provisional application has withdrawn Claims 1-4 and 17-28 drawn to a nonelected invention without traverse in the reply filed on 25 May 2006 in response to Election/Restriction requirement in the Office Action mailed 04 May 2006. A complete reply to the instant final rejection must include cancellation of nonelected claims, or other appropriate action (See, 37 C.F.R. §1.144 and M.P.E.P. §821.01).

Claims Status

7. According to the list of Claims presented with response and amendment filed 19 September 2008 cited *supra,* following is the current status of Claims:

- Claims 8-16 and 29-30 currently remain cancelled;
- Claims 1-7, 17-28 and 31 are currently pending;
- Claims 1-4 and 17-28 remain withdrawn;
- Claims 5 and 31 have currently been amended; and

- Claims 5-7 and 31 are currently under examination.

8. Claims 5-7 and 31 are examined on merits.

Claim Rejections - 35 U.S.C. §112, First Paragraph

9. The following is a quotation of the first paragraph of 35 U.S.C. §112:

> *The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

10. Claims 5 and 7 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention and further lack of enablement with respect to the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with those claims (See Office Action mailed 01 May 2008, Pages 3-4, item 11).

In response filed 19 September 2008 to the above recited rejection to Claims 5-7 in the Office Action mailed 01 May 2008, the presented argument is, "Regarding the rejection under 35 U.S.C. §112, Claim 5, and hence all Claims, now requires the claimed peptide consists of 10-12 amino acids". Applicants recite a number of citations to the specification to indicate that the currently presented specification supports said amendment to the Claims. Applicants also present the argument, ""it's the Examiner's burden to make out a prima faciae case. While the Examiner is alleging that the rejection is one based on written description, it is not. It is an enablement rejection, and a specification is presumed to be enabled. The burden is on the Examiner and mere conclusory statements do not make out a *prima faciae* case. The rejection is improper" (See, Remarks filed 19 September 2008, Page 7, Lines 11-24).

Contrary to Applicants' assertion recited above, the above-cited rejection to Claims 5-7 and 31 under 35 U.S.C. §112, first paragraph is not improper. Upon closer examination of the wordings in Paragraphs 1-2 of said rejection, applicants will find that applicants are correct in stating that said rejection "is an enablement rejection". In fact said rejection is an enablement and a written description rejection; because the instantly presented specification in its current form does not clearly demonstrate the antimicrobial functionality of the claimed peptide at the citations that applicants argue with (i.e., Page 9, Line 13 to Page 10, Line 21; Figures 3A-3C and

Example 3, at page 43 at seq.). This is because antimicrobial activity of a compound or material is defined as either microbicidal, or microbistatic. This means that the antimicrobial substances either prevent the growth of microbes or kill the microbes (See Wikipedia, modified 30 December 2008, at 01:04, http://en.wikipedia.org/wiki/Antimicrobial, printed on 02 January 2009). However, at the specifically recited paragraphs of the currently presented specification, especially at Page 9, Line 13 to Page 10, Line 21 and in Example 3 membrane damage is demonstrated not destruction or slowing down of the microbial cell. Thus, the currently provided description in the specification as currently presented, neither enables the applicants' claimed invention commensurate with Claims 5-7 and 31, nor shows that applicants had in their possession of instantly claimed invention in Claims 5-7 and 31 at the time the instant application was filed.

Applicants' arguments filed 19 September 2008 regarding the written description and enablement of scope rejection of Claims 5-7 and 31 under 35 U.S.C. §112, 1st Paragraph in the Office Action mailed 01 May 2008 have been fully and carefully considered but are not persuasive for the reasons of record at pages 3-4, item11 in the Office Action mailed 01 May 2008 and those discussed *supra*. Thus, the rejection of Claims 5 and 7 and consequently of Claims 5-7 and 31 under 35 U.S.C. §112, 1st Paragraph in the Office Action mailed 01 May 2008 is maintained and is adhered to; because Claims 6 and 31 directly or indirectly depend from Claim 5.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention of*

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR §1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § *103*(c) and potential 35 U.S.C. § *102*(f) or (g) prior art under 35 U.S.C. § 103(a).

13. Claims 5-7 and 31 are rejected under 35 U.S.C. §103 (a) as obvious over the combined teachings from Ford et al. (US Patent 6,497,870 B1) in view of Hancock et al (US Patent 6,040,435) and further in view of Aley et al (Infection and Innunity, 1994, Volume 62, pages 5397-5403).

Claims 5-7 and 31 recite an isolated antimicrobial amidated, carboxymethylated or cyclized peptide consisting of from 10-12 amino acid residues, wherein 7 amino acid residues are hydrophobic, 3 are basic and at least one is one among histidine09, glutamic acid or serine with two of the hydrophobic residues comprised of adjacent tryptophan residues. Additionally, said peptide comprises amino acid sequence set forth in SEQ ID NO: 1, 2, 3, or 4.

Regarding Claims 5-7 and 31, Ford et al teach a polypeptide having the amino acid sequence of SEQ ID NO: 1 or an active variant thereof that differs from the natural polypeptides by amino acid insertion, deletion and substitutions, said variants having up to 95% or higher sequence identity to SEQ ID NO: 1 and retained the biological activity. (Column 8, Lines 8-20). Ford et al. further teach replacement of said amino acid residues having similar structure/function relationships and are therefore conservative replacements. Among the conservative properties for amino acid residues to be substituted, Ford et al teach hydrophobicity, hydrophilicity, amphipathy of substituted residues and further teach at least 7 hydrophobic residues, additionally serine and histidine and also tryptophan (Column 8, Lines 3045; Column. Thus, Ford et al teach a polypeptide comprised of same amino acid residues and having same structure functional relationship as is instantly claimed. Ford et al., however, are silent about said isolated peptide to be antimicrobial and amidated, carboxymethylated or cyclized and exhibiting low toxicity to animal and plant cells.

Hancock et al. teach a peptide comprising 20 amino acids. Said peptide comprises 10-12 contiguous amino acids, wherein at least 7 of those amino acids are hydrophobic, at least 3 are basic, at least one is serine and two of hydrophobic amino acids are tryptophan adjacent to each other (See Column 11, Lines 34-55 and illustration below).

NH_2 –KK **WW**RRVL**S**GLKTG PALSNV-COOH, (20 amino acid residues)
1 2 3 4 5 6 7 8 9 1011 12
h h h h h h h
b b b

Above illustration, as an example indicates a total of 20 amino acid residues. Among 12 of said contiguous amino acid residues, 7 are hydrophobic (indicated by h), 3 basic (indicated by b), at least one serine (indicated by S) and two adjacent tryptophan (indicated by W).

Other examples are shown below.

NH_2–KK**WW**RRVLKGLSSG PALSNV-COOH,

NH_2-KK**WW**RRALQALKNG PALSNV-COOH,

NH_2-KK**WW**RRVLSGLKTA GPAIQSVLNK-COOH,

NH_2-KK WWRRALQGLKTA GPAIQSVLNK-COOH,

NH_2-KK WWKAQKAVNSGP NALQTLAQ-COOH,

NH_2-KK WWKAKKFANSGP NALQTLAQ-COOH,

NH_2-KK WWKFIKKAVNSG TTGLQTLAS-COOH,

Hancock et al., further teach, isolated antimicrobial peptides of at least 20-30 amino acid length (Column 5, Lines 33-34) analogs derivatives and conservative variations of said peptides having hydrophobic substitutions (Column 4, Lines 29-34; Lines 58-63) and thus said peptides inherently are amidated, carnoxymethylated, or cyclized (amidation of the dodecamer can be the remaining peptide fused to the C-terminus; in the example above, it is PALSNV-COOH).

Aley et al. teach isolated antimicrobial polypeptide, i.e., defensins and indolicidins that have nine highly conserved amino acid residues (Page 5397, Column 1, Lines 38-43; are uniquely tryptophan rich (Abstract Lines 15-16) and additionally has C-terminal amide (Page 5397, Column 2, Lines 31-34). Aley et al. further teach that said polypeptides have conservative substitutions, have amphipathic surface topology (Page 5400, Column 2, below Figure 4, Lines 5-15). Thus, combined teachings from Ford et al., Hancock et al., (US Patent 6,040,435) and Aley et al., teach an isolated antimicrobial peptide having each of the limitations that the instant Claims 5-7 and 31 have. Therefore, the prior art isolated antimicrobial peptide is comprised of the same amino acid constituents as are instantly claimed (See e.g., *In re Best*, 195 USPQ 430, 433-CCPA 1977).

One having ordinary skill in the art at the time of the claimed invention would have been motivated to modify/combine the teachings from Ford et al., with those from Hancock et l., and Aley et al's to obtain the claimed antimicrobial, polypeptide having the amino acid sequence of SEQ ID NO: 1; because Hancock et al., teach isolated antimicrobial peptides of at least 20-30 amino acid length, analogs derivatives and conservative variations of said peptides having hydrophobic substitutions, and thus said peptides intrinsically are amidated, carnoxymethylated, or cyclized Among 12 of said contiguous amino acid residues, 7 are hydrophobic, 3 basic, at least one serine and two adjacent tryptophan and Aley et al.,

teach, defensins and indolicidins are isolated antimicrobial peptides and said peptides are rich in tryptophan, have at least 9 highly conservative amino acid residues and amidated c-terminus thereof .

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify Ford et al's teachings with those from Hancock et al., and Aley et al's to obtain the claimed antimicrobial, polypeptide having the amino acid sequence of SEQ ID NO: 1; because Hancock et al., teach isolated antimicrobial peptides of at least 20-30 amino acid length, analogs derivatives and conservative variations of said peptides having hydrophobic substitutions. Hancock et al., further teach, among 12 of said contiguous amino acid residues, 7 are hydrophobic, 3 basic, at least one serine and two adjacent tryptophan and Aley et al., teach, defensins and indolicidins are isolated antimicrobial peptides and said peptides are rich in tryptophan, have at least 9 highly conservative amino acid residues and amidated c-terminus thereof. Thus, combined teachings from Ford et al., Hancock et al., (US Patent 6,040,435) and Aley et al., teach an isolated antimicrobial peptide having each of the limitations that the instant Claims 5-7 and 31 have.

From the teachings of the references cited *supra*, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

15. Applicant's amendment filed 19 September 2008 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP §706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. For the aforementioned reasons, no claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923. The examiner can normally be reached on Monday to Thursday from 7:30 A.M. to 6:00 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached at (571)-272-0925 Monday through Thursday 7:30 A.M. to 6:00 P.M. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding may be obtained from the Patent Application Information Retrieval (i.e., PAIR) system. Status information for the published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (i.e., EBC) at: (866)-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Examiner, Art Unit 1657

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